

**APPENDIX H:
SUPPORT¹ FOR THE CLAIMS OF THE PRESENT APPLICATION
IN THE DISCLOSURE OF THE PRESENT APPLICATION**

New Claim	Support in the Present Application (09/589,288)
<p>195. A method of inhibiting B lymphocytes comprising administering an effective amount of an antibody that binds a protein whose amino acid sequence is:</p> <p style="margin-left: 40px;">MDDSTEREQS RLTSCLKKRE EMKLKECVSI LPRKESPSVR SSKDGKLLAA TLLLALLSCC LTVVSFYQVA ALQGDLASLR AELQGHHA EK LPAGAGAPKA GLEEAPAVTA GLKIFEPPAP GEGNSSQNSR NKRAVQGPEE TVTQDCLQLI ADSETPTIQK GSYTFVPWLL SFKRGSAL EE KENKILVKET GYFFIYGQVL YTDKTYAMGH LIQRKKVHVF GDELSLVTLF RCIQNMPETL PNNSCYSAGI AKLEEGDELQ LAIPRENAQI SLDGDVTFFG ALKLL</p> <p>wherein B lymphocytes are inhibited.</p>	<p>“Like other members of TNF family, Neutrokin e-alpha exhibits activity on leukocytes including, for example, monocytes, lymphocytes (e.g., B cells) and neutrophils. For this reason Neutrokin e-alpha is active in directing the proliferation, differentiation and migration of these cell types.” <i>p. 83:7-10</i></p> <p>“The antagonists may be employed for instance to inhibit Neutrokin e-alpha-mediated and/or Neutrokin e-alphaSV-mediated chemotaxis and activation of macrophages and their precursors, and of neutrophils, basophils, B lymphocytes and some T-cell subsets, e.g., activated and CD8 cytotoxic T cells and natural killer cells, in certain auto-immune and chronic inflammatory and infective diseases.” <i>p. 331:15-19</i></p> <p>“A still further embodiment of the invention is related to a method for treating an individual in need of a decreased level of Neutrokin e-alpha and/or Neutrokin e-alphaSV activity in the body comprising, administering to such an individual a composition comprising a therapeutically effective amount of an Neutrokin e-alpha and/or Neutrokin e-alphaSV antagonist. Preferred antagonists for use in the present invention are Neutrokin e-alpha-specific and/or Neutrokin e-alphaSV-specific antibodies.” <i>p. 24:10-15</i></p> <p>“Additionally, as described in detail below, the polypeptides of the present invention have uses that include, but are not limited to, to raise polyclonal and monoclonal antibodies, which are useful in assays for detecting Neutrokin e-alpha and/or Neutrokin e-alphaSV polypeptide expression as described below or as agonists and antagonists capable of enhancing or inhibiting Neutrokin e-alpha and/or Neutrokin e-alphaSV function.” <i>p. 223:17-22</i></p> <p>“Preferred antagonists for use in the present invention are Neutrokin e-alpha-specific and/or Neutrokin e-alphaSV-specific antibodies.” <i>p. 24:14-15. See also p. 429:13 - p. 433:2</i></p> <p>“An agonist is a compound which increases the natural</p>

¹ This table shows exemplary support for the indicated claims in Application No. 09/589,288. Applicants reserve the right to supplement this table as necessary.

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	<p>biological functions of Neutrokin-alpha and/or Neutrokin-alphaSV or which functions in a manner similar to Neutrokin-alpha and/or Neutrokin-alphaSV while antagonists decrease or eliminate such functions.” <i>p. 366:12-15</i></p> <p>“Figures 1A and 1B shows the nucleotide (SEQ ID NO:1) and deduced amino acid (SEQ ID NO:2) sequences of Neutrokin-alpha.” <i>p. 24:19-20</i></p>
<p>196. A method of inhibiting B lymphocyte proliferation comprising administering an effective amount of an antibody that binds Neutrokin-alpha (SEQ ID NO:2), wherein B lymphocyte proliferation is inhibited.</p>	<p><i>See support for Claim 195</i></p>
<p>197. A method of inhibiting B lymphocyte differentiation comprising administering an effective amount of an antibody that binds Neutrokin-alpha (SEQ ID NO:2), wherein B lymphocyte differentiation is inhibited.</p>	<p><i>See support for Claim 195</i></p>
<p>198. The method of any one of claims 195-197, wherein the antibody is a monoclonal antibody.</p>	<p><i>See support for Claim 195 and in addition, the following disclosure:</i></p> <p>“Antigenic epitope-bearing peptides and polypeptides of the invention are therefore useful to raise antibodies, including monoclonal antibodies, that bind specifically to a polypeptide of the invention.” <i>p. 114:13-15</i></p> <p>“The term “antibody” (Ab) or “monoclonal antibody” (mAb) as used herein is meant to include intact molecules as well as fragments thereof (such as, for example, Fab and F(ab') fragments) which are capable of binding an antigen.” <i>p. 376:23-25</i></p> <p>“In a preferred method, antibodies according to the present invention are mAbs. Such mAbs can be prepared using hybridoma technology (Kohler and Millstein, <i>Nature</i> 256:495-497 (1975) and U.S. Patent No. 4,376,110; Harlow et al., <i>Antibodies: A Laboratory Manual</i>, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1988; <i>Monoclonal Antibodies and Hybridomas: A New Dimension in Biological Analyses</i>, Plenum Press, New York, NY, 1980; Campbell, “Monoclonal Antibody Technology,” In: <i>Laboratory Techniques in Biochemistry and Molecular Biology</i>,</p>

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	Volume 13 (Burdon et al., eds.), Elsevier, Amsterdam (1984)).” p. 377:3-10
199. The method of any one of claims 195-197, wherein the antibody is recombinantly produced.	See support for Claim 195 and in addition the following disclosure: “Methods of Producing Antibodies The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.” p. 243:21-24
200. The method of any one of claims 195-197, wherein the antibody is a chimeric antibody.	See support for Claim 195 and in addition the following disclosure: “Where <i>in vivo</i> imaging is used to detect enhanced levels of Neutrokin- α and/or Neutrokin- α SV polypeptide for diagnosis in humans, it may be preferable to use human antibodies or “humanized” chimeric monoclonal antibodies. Such antibodies can be produced using techniques described herein or otherwise known in the art. For example methods for producing chimeric antibodies are known in the art. See, for review, Morrison, <i>Science</i> 229:1202 (1985); Oi et al., <i>BioTechniques</i> 4:214 (1986); Cabilly et al., U.S. Patent No. 4,816,567; Taniguchi et al., EP 171496; Morrison et al., EP 173494; Neuberger et al., WO 8601533; Robinson et al., WO 8702671; Boulianne et al., <i>Nature</i> 312:643 (1984); Neuberger et al., <i>Nature</i> 314:268 (1985).” p. 307:7-16
201. The method of any one of claims 195-197, wherein the antibody is a humanized antibody.	See support for Claims 195 and 200
202. The method of any one of claims 195-197, wherein the antibody comprises human constant domains.	See support for Claims 195 and 200
203. The method of any one of claims 195-197, wherein the antibody is a F(ab') ₂ fragment.	See support for Claim 195 and in addition the following disclosure: “The term “antibody” (Ab) or “monoclonal antibody” (mAb) as used herein is meant to include intact molecules as well as fragments thereof (such as, for example, Fab and F(ab') fragments) which are capable of binding an

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	<p>antigen.” <i>p. 376:23-25</i></p>
<p>204. The method of any one of claims 195-197, wherein the antibody is a polyclonal antibody.</p>	<p><i>See support for Claim 195 and in addition the following disclosure:</i></p> <p>“Polyclonal antibodies to an antigen-of-interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen.” <i>p. 234:15-19</i></p>
<p>205. The method of any one of claims 195-197, wherein the antibody is a Fab fragment.</p>	<p><i>See support for Claims 195 and 203</i></p>
<p>206. The method of any one of claims 195-197, wherein the antibody is administered to an individual.</p>	<p><i>See support for Claim 195 and in addition the following disclosure:</i></p> <p>“The agonists and antagonists may be employed in a composition with a pharmaceutically acceptable carrier, e.g., as described herein.” <i>p. 331:13-14</i></p> <p>“The agonists and antagonists of the instant may be employed in a composition with a pharmaceutically acceptable carrier, e.g., as described hereinafter.” <i>p. 338:18-19</i></p>
<p>207. The method of any one of claims 195-197, wherein the antibody is administered to a cell culture.</p>	<p><i>See support for Claim 195 and in addition the following disclosure:</i></p> <p>“The invention also provides a method of screening compounds to identify those which enhance or block the action of Neutrokin-α and/or Neutrokin-αSV polypeptide on cells, such as its interaction with Neutrokin-α and/or Neutrokin-αSV binding molecules such as receptor molecules. An agonist is a compound which increases the natural biological functions of Neutrokin-α and/or Neutrokin-αSV or which functions in a manner similar to Neutrokin-α and/or Neutrokin-αSV while antagonists decrease or eliminate such functions.” <i>p. 366:9-15</i></p> <p>“An <i>in vitro</i> cell proliferation, cytotoxicity, cell survival,</p>

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	<p>and cell death assay for measuring the effect of a protein on certain cells can be performed by using reagents well known and commonly available in the art for detecting cell replication and/or death....Such cell proliferation and/or survival modulation activities as can be measure in this type of assay are useful for treating tumor, tumor metastasis, infections, autoimmune diseases, inflammation and other immune-related diseases.”</p> <p><i>p. 82:4-15</i></p>